FDA Oversight of New Glucose Diagnostic Devices

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MEDICAL DEVICE AMENDMENTS OF 1976

General Controls

- Register and List
- Follow good manufacturing practices
- Report device failures

General Controls

- Inventory of tests on the market
- Tools to require good manufacturing practices
- System for remedying device failures

Premarket Review

- Division of Clinical Laboratory Devices (DCLD)
- 60 scientists

Submissions Reviewed

- Premarket Notification 510(k)s
- Premarket Approvals (PMAs)

Semantic Framework

- Old vs. New
- In vitro diagnostic devices

510(k)s

- ~ 500 submissions/year
- Substantially equivalent
- Comparisons to predicate device
- Standard glucose meters
- Standard glucose measures

510(k) Reviews

- Accuracy
- Precision
- Analytical sensitivity
- Analytical specificity
- Key elements for standard glucose meter in ISO/TC 212

Limitations in Review

- Paper review
- Lack of performance standards

PMA Review

- ~ 6 - 12 applications/year
- Safety and Effectiveness
- Non-invasive and minimally invasive glucose monitors

Clinical Performance Characteristics

- Clinical sensitivity
- Clinical specificity
- Predictive values

Limitations of Review

- Lack of “gold standards”
- Overt and latent bias
- Lack of performance standards

Labeling of in vitro diagnostic devices 809.10(b)

- Proprietary and established names
- Intended Use(s)
- Summary and explanation of test
- Principle of procedures

Labeling 809.10(b) (continued)

- Information on reagents
- Information on instruments
- Information on specimen collection and preparation

Labeling 809.10(b) (continued)

- Procedures
- Results
- Limitations of the procedure

Labeling 809.10(b) (continued)

- Expected values
- Specific performance characteristics
- Bibliography
- Name and place of business
- Date of the package insert

Intended Use

- Type of review
- Questions raised
- Data required

Scientific Model

- Literature
- Voluntary Standards
- FDA guidances

Development of a Scientific Model

- Upfront design of the study
- Careful and meticulous collection of data
- Sound interpretation of results

FDA Review

- Not outcome oriented
- Usually concurrent not prospective
- Good science

New Glucose Devices

- New issues of safety and effectiveness
- Analytical issues are different
- Calibration and QC issues are different
- Biological issues are different

Challenges in Study Design

- Conflict between lab truth and real world use
- Conflict between lab truth and physiological truth
- Uncertain risk benefit ratio in possibility of increased information but of more unpredictable quality

Methods of Data Analysis

- Traditional regression analysis using quantiative statistical models
- More modern clinical models for estimating impact of results -- Clarke Error Grid and others
- Impact of partioning on both forms of analysis

FDA Data Requirements

- Evaluation of data in relevant clinical zones
- Evaluation of trends and pattern
- Appropriate labeling to ensure safe and effective use

FDAMA

- Improved market access
- Least burdensome pathways
- Premarket to postmarket balance
- Increased interaction with industry

Least Burdensome

- Appropriate questions
- Appropriate thresholds
- Non-academic pursuits

Least Burdensome

- Matter of law
- Matter of policy
- Matter of spirit

Increased Interactions

- Formal meeting process
- Formal agreement process
- Formal process for dealing with disagreements

Total Product Life Cycle

- Cradle to grave
- Seamless oversight
- Incorporates other elements

Intellectual Appeal

- Premarket Review limitations
- Law -- 510(k), PMAs
- Snapshot approach
- Impact of scale-up
- Impact of wide use

Quality System

- Require quality assessment
- Require process controls
- Require corrective actions

OIVD Program

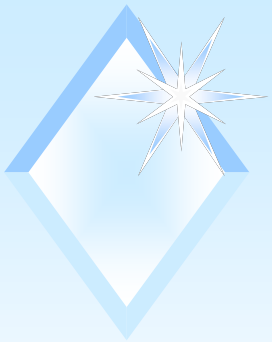
- New office -- Office of In Vitro Diagnostic Device Evaluation and Safety
- Combines pre and post market work into a single functional unit
- Allows for global regulation across the total product life cycle

Ideal Candidate

- Stereotyped analytical approach
- Cadre of devoted scientists
- History of incomplete connections
- Interested and cohesive partners
- Need to foster technology transfer

FDA Dual Mission

- Allow rapid access to good new technology
- Prevent bad products from being marketed
- Obvious inherent tension
- OIVD a possible solution



GOOD SCIENCE